REMARKS

Applicant thanks the Examiner for meeting with Applicant's counsel, Daniel Altman and Salima Merani and the inventor, Dr. Guru Betageri. The claim amendments and remarks herein are responsive to the Office Action dated January 9, 2003 and fully incorporate the Examiner's suggestions during the Interview. Claims 1-12 have been canceled without prejudice. Claims 13-40 are pending.

Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected Claims 8, 13-23 and 35 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that the distinction between the terms "liquid" and "suspensions" recited in Claims 8, 13 and 35 is unclear. The Examiner suggested that Applicant delete the term "liquid." Because liposomes in an aqueous solution are by definition a "suspension" and because the term "suspension" includes liquids, Applicant has deleted the term "liquid."

In light of Applicant's amendments, Applicant respectfully submits that the claims are in compliance with 35 U.S.C. § 112, second paragraph.

Provisional Rejection for Double Patenting

The Examiner provisionally rejected Claims 1-12 and 37-38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 14-39 and 41-60 of co-pending Application No. 09/562,207. Applicant has canceled Claims 1-12 without prejudice. Applicant has also amended Claims 37-38 to depend from Claim 13, an allowable base claim.

Accordingly, in light of Applicant's amendments, Applicant respectfully requests that the Examiner withdraw the provisional rejection for double patenting.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected Claims 1-38 under 35 U.S.C. §102(b) as anticipated by U.S. Pat. No. 5,206,219 to Desai.

Applicant respectfully asserts that Desai does not teach or suggest the formation of proliposomes. As described in Applicant's specification, proliposomes are dry, free-flowing granular products, which, upon the addition of water, disperse to form a multilamellar liposomal suspension. Desai only teaches the formation of a *microemulsion.* Moreover, because Desai's formulation is a microemulsion, it does not form liposomes at the absorption site. Accordingly, Desai requires absorption enhancers and co-solvents to facilitate absorption of the microemulsion. By contrast, Applicant's formulation comprises proliposomes pre-ingestion and forms liposomes at the absorption site. Because liposomes are easily absorbed, Applicant's formulation does not require absorption enhancers or co-solvents. Accordingly, Applicant has amended Claims 13 and 24 to reflect the formation of *proliposomes* pre-ingestion (as opposed to Desai's microemulsion). Claims 13 and 24 now explicitly recite the production of "a proliposomal combination."

Further, Desai does not teach or suggest the enteric coating of a phospholipid. Indeed, Desai only teaches encapsulating or packing a pre-emulsion solution into a capsule which has been coated with an enteric coating. In other words, Desai coats the final product, i.e. the capsule, and does not coat the proliposomes (or micro-emulsion). By contrast, Applicant's method involves coating the proliposomes, and, as such, the enteric coating is in contact with the proliposomes. Coating the proliposomes, instead of the capsule, has several advantages. For example, coating the proliposome powder is easier and less expensive than coating a bulkier capsule or end-product. Accordingly, Applicant has amended Claims 13 and 24 to reflect that the enteric coating coats the proliposomes. Claims 13 and 24 now recite an enteric coating, "wherein said enteric coating is in contact with at least a portion of said proliposomal combination."

In view of the above comments, Applicant respectfully requests withdrawal of the § 102(b) rejection of independent Claims 13 and 24 and all claims which depend therefrom, specifically Claims 14-23 and 25-36.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected the Claims under 35 U.S.C. § 103(a) as being unpatentable over Nakagame (U.S. Pat. No. 4,615,885) in view of Ganter (U.S. Pat. No. 5,635,206). Applicant respectfully submits that there is no motivation to combine Nakagame with Ganter. Moreover, even assuming that Nakagame is properly combined with Ganter, Nakagame still does not render Applicant's claims obvious. Embodiments of Applicant's invention are patentable over Nakagame because Applicant's method uses a single-step process which does not expose the pharmaceutical agent to an aqueous phase. As described below, Applicant's method produces surprising and unexpected results.

The Examiner suggested that Applicant perform both Applicant's method and Nakagame's method of preparing formulations and compare the properties of the product produced by each method.

In accordance with the Examiner's suggestion, the inventor, Dr. Guru Betageri, prepared proliposomal formulations using Applicant's method and the method disclosed by Nakagame. The results of this comparison study are shown in Exhibit A. Exhibit A is a copy of the Declaration submitted by Dr. Guru Betageri under 37 C.F.R. § 1.132.

Applicant performed the comparison study and assessed three different parameters: (1) the percent yield obtained for each drug (2) the concentration obtained for the final product and (3) the color of the final product. Results for the following five drugs are provided: nicotinamide, benzocaine, hydrochlorothiazide, aspirin, and erythromycin.

Table 1 of Exhibit A shows that the percent yield using Applicant's method and Nakagame's method. Of the five drugs tested, Applicant's method was significantly better than Nakagame's method for four of the five drugs. For one drug, hydrochlorothiazide, Applicant's method performed substantially the same as Nakagame's method. Indeed, the average percent yield with Applicant's method was 95%, while Nakagame's method provided only a 65% percent yield. Thus, Applicant's method provides surprising and unexpected results. Because Applicant's method does not expose the drug to an aqueous phase and uses only a one-step process, the percent yield for the drugs is significantly higher than the yield obtained by the Nakagame method.

Table 2 of Exhibit A shows that the final concentration of the drug obtained using Applicant's method and Nakagame's method. Equivalent amounts of each drug were prepared using the two methods and final concentration was assayed via an absorbance assay. This concentration comparison assay showed that Applicant's method yielded a concentration that was 86% higher than that obtained using Nakagame's method. Thus, once again, Applicant's method provides surprising and unexpected results. Because Applicant's method does not expose the drug to a damaging aqueous phase, the production yield for the drugs is significantly higher than the yield obtained by the Nakagame method.

Table 3 of Exhibit A shows a qualitative comparison of the end-product obtained using Applicant's method and Nakagame's method. Nakagame's method resulted in a discolored product for all but one of the drugs tested. By contrast, Applicant's method resulted in a white powder. The discolored products obtained using Nakagame's method indicates degradation of the drug. Attached herewith as Exhibit B is an excerpt from a textbook entitled "Stability of Drugs and Dosage Forms" that provides that discoloration is consistent with a degraded product. Therefore, because Applicant's method does not expose water-labile and water-sensitive drugs to an aqueous phase, Applicant's method provides surprising and unexpected results by preserving the integrity of those drugs.

In view of the above technical results and discussion, Applicant respectfully requests withdrawal of the § 103(a) rejection of Claims 1-38.

CONCLUSION

In view of the foregoing remarks, Applicant respectfully asserts that the present application is fully in condition for allowance. If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number indicated below.

Appropriate fees have been submitted herewith. No further fees are believed to be due. However, please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: 9 July 2003

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